

Message

**From:** Elizabeth Erwin [Erwin.ElizabethLNDU@usepa.onmicrosoft.com]  
**Sent:** 1/20/2011 5:57:32 PM  
**To:** Clark, Becki [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a906e07f1cd143b9a3c2ddab813b8140-Clark, Becki]; Flowers, Lynn [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=1a4411c874d041b9a8badfc32b91bd70-Flowers, Lynn]; Michael Slimak [Slimak.MichaelLNDU@usepa.onmicrosoft.com]; Barone, Stan [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a4f8618acbb418da24c110f3123a2af-Barone, Stan]; CN=Linda Tuxen/OU=DC/O=USEPA/C=US@EPA; Ila Cote [Cote.IlaLNDU@usepa.onmicrosoft.com]; Jones, Samantha [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=eac77fe3b20c4667b8c534c90c15a830-Jones, Samantha]; Birchfield, Norman [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c910f2fd28414e819b6afe6dda525e9f-Birchfield, Norman]; Avery, James [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b0fc9e70467647709fa9377dfb987f10-Avery, James]; Anne Grambsch [Grambsch.AnneLNDU@usepa.onmicrosoft.com]; Shaw, Denise [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=556182b3879649039b11d36e5e09d9aa-Shaw, Denise]; CN=Madalene Stevens/OU=DC/O=USEPA/C=US@EPA; Kadry, Abdel-Razak [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=acb325507bf7451b9735813cfd5e417-Kadry, Abdel-Razak]; Karen Hammerstrom [Hammerstrom.KarenLNDU@usepa.onmicrosoft.com]; Bussard, David [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cf26b876393e44f38bdd06db02dbbfe5-Bussard, David]; Charles Ris [Ris.CharlesLNDU@usepa.onmicrosoft.com]; Perovich, Gina [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=6e3c19d7f4db41bfa2477aa27ad83945-Perovich, Gina]; White, Paul [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4e179825823c44ebbb07a9704e1e5d16-White, Paul]; Bob Sonawane [Sonawane.BobLNDU@usepa.onmicrosoft.com]; Frithsen, Jeff [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e3743bd6f3c345baaae407c1d6f78e92-FRITHSEN, JEFF]; Gatchett, Annette [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f12d699a71f84e21bddbb876dae7f96c-Gatchett, Annette]; Hawkins, Belinda [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=075561d171e845828ec67a945663a8e6-Hawkins, Belinda]; Troyer, Michael [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=847b0020dd0e457e85f994a1ad64b26d-Troyer, Michael]; Vandenberg, John [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dcae2b98a04540fb8d099f9d4dead690-Vandenberg, John]; Debra Walsh [Walsh.DebraLNDU@usepa.onmicrosoft.com]; Sams, Reeder [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7d5b479ccd894cea99ae55df20de6971-Sams, Reeder]; Ross, Mary [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=98359cd1f66f46ec91d327e99a3c6909-Ross, Mary]; Strong, Jamie [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ea753aafefb74c268550fe6a2c187838-Benedict, Jamie]; Hotchkiss, Andrew [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=10f01ccc8611401bb34d16b71a87d3d5-Hotchkiss, Andrew]; Rieth, Susan [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=00aac63cc995489188b8a449aaa18f5e-Rieth, Susan]; Martin Gehlhaus [Gehlhaus.MartinLNDU@usepa.onmicrosoft.com]; Raffaele, Kathleen [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cc48281bbab34bf5bf3ab1a63780d5ca-Kathleen Raffaele]; Berner, Ted [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f1949c9653024d3cb4aa4c2bd69c4fde-Berner, Ted]; Peter Preuss [Preuss.PeterLNDU@usepa.onmicrosoft.com]; Deener, Kathleen [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b9a2ff1c086249ea8f6414afde8a5e54-Deener, Kathleen]; Winner, Darrell [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=860556f5cd0f4855839907bcc90b2c41-Winner, Darrell]; Murphy, Patricia [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4e02a7540f8042fda07eed1248addaf7-Murphy, Patricia]; Weihsueh Chiu

[Chiu.WeihsehLNDU@usepa.onmicrosoft.com]; Corona, Elizabeth [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=18d86fb8269b4557b5d06622b3a941af-Corona, Elizabeth]; Elizabeth Erwin [Erwin.ElizabethLNDU@usepa.onmicrosoft.com]; Cogliano, Vincent [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=51f2736376ac4d32bad2fe7cfef2886b-Cogliano, Vincent]; CN=Audrey Hoffer/OU=DC/O=USEPA/C=US@EPA; Gwinn, Maureen [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4bdc5237a5c440a7b664518e23eb5647-Gwinn, Maureen]; CN=Doug Johns/OU=RTP/O=USEPA/C=US@EPA

**Subject:** NEWS UPDATES: EPA Seeks To Expand Review Of Controversial Lab Data In Key Risk Studies (InsideEPA)

# EPA Seeks To Expand Review Of Controversial Lab Data In Key Risk Studies

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EPA is seeking a broader review of controversial Italian laboratory data the agency has relied on in several major chemical risk assessments but which officials placed on hold last summer after a preliminary review by National Toxicology Program (NTP) pathologists raised questions about the Ramazzini Institute's methods and results.

An EPA spokeswoman says agency staff are discussing plans with staff at the National Institute of Environmental Health Sciences (NIEHS), which houses NTP, to perform a full pathology working group (PWG) review of certain Ramazzini studies.

The effort could further delay some or all of the six Integrated Risk Information System (IRIS) risk assessments placed in limbo by EPA's announcement last June that it is reviewing the assessments because they contain Ramazzini data. PWG reviews are intensive and expensive: a group of pathologists reviews the original tissue slides taken from lab animals and votes on whether each is cancerous or non-cancerous. In this manner, they would review all of the data collected in the study.

But some industry sources are questioning whether the Ramazzini Institute will allow such a review of its data.

EPA last summer halted progress on four ongoing draft assessments that contained Ramazzini data -- including those of methanol, the fuel additives methyl tertiary butyl ether (MTBE) and ethyl tert-butyl ether (ETBE), and the plastic ingredient acrylonitrile -- as well as existing assessments of vinyl chloride and 1,1 dichloroethylene (DCE), which were published on the IRIS website in 2000 and 2002 respectively (*Inside EPA*, June 18).

IRIS assessments are important because of their role as the basis for many regulatory standards and decisions in all environmental media.

The agency pulled the assessments due to a report from NTP that raised questions about the results and methods of Ramazzini's studies on methanol's carcinogenicity and found a lower incidence of lymphoma or leukemia in Ramazzini's test rats exposed to methanol than what Ramazzini scientists found. Industry groups have also raised concerns about some of the draft assessments that EPA pulled, including methanol and ETBE, in part because their reliance on Ramazzini data made the chemicals appear more toxic than industry stakeholders thought the assessments should.

Industry has long urged EPA to either drop its use of the Ramazzini data, or perform full PWG reviews of its data. Most recently, several industry associations petitioned EPA to seek PWG reviews of all of the Ramazzini studies EPA references in five of the six assessments, or drop the studies from the assessments. The associations -- among them American Forest & Paper Association, American Petroleum Institute and the Methanol Institute -- filed the petition regarding the acrylonitrile, ETBE, DCE, methanol and vinyl chloride assessments, leaving out the MTBE assessment due to ongoing litigation over the chemical's appearance in groundwater (*Inside EPA*, Aug. 13).

While speedy review of IRIS assessments is a top priority for EPA Administrator Lisa Jackson, agency officials say they are now considering a broader pathology review of the Ramazzini data. "EPA and NIEHS are in detailed conversations, and plan to jointly sponsor an independent [PWG] review of select studies conducted at the institute. The specifics regarding the scope and plan for the PWG work will be made available publicly in the near future," an EPA spokeswoman tells *Inside EPA*.

The spokeswoman explains that EPA decided to seek the further PWG review because the June NTP report "recommended that further pathology reviews be carried out to resolve differences of opinion between NTP scientists and the Ramazzini Institute in the diagnoses of certain tumors reported in the methanol study."

In its report, NTP cautioned that its review was preliminary and considered only one Ramazzini study of the chemical methanol. Some observers last summer questioned why EPA pulled all of its assessments containing Ramazzini data rather than just the methanol assessment containing that study. Now, EPA is seeking a fuller pathology review all of the Ramazzini studies.

**But one industry source questions whether Ramazzini will allow for this type of broader review**, saying, "I don't see what's in it for the Ramazzini Institute." Industry and its consultants have in the past sought to perform such reviews of Ramazzini's work, without success.

In an interview last spring, Morando Soffritti, Ramazzini's science director, did not address whether he would agree to a PWG but reiterated his laboratory's close cooperation with federal officials. He described NTP pathologists' initial visit last year to perform the preliminary review as "further evidence of the very close collaboration built over the years" between Ramazzini and NTP.

"This is the third or fourth time NTP is coming for a collegial meeting; it is a normal part of our procedure working together. It is not a reaction to the [EPA IRIS] methanol review," he added (*Inside EPA*, June 18).

Observers last summer expected that EPA's announcement would result in significant delays for two of the six assessments -- methanol and vinyl chloride -- because EPA relied on Ramazzini data to set numeric cancer risk levels for these two chemicals. The industry source suggests that, at least in the case of methanol, the PWG may be the only way forward for EPA, because there are only four methanol cancer bioassays: two published by a Japanese industry association, a Finnish graduate student's thirty-year-old dissertation and the Ramazzini study. "It does make sense for them to pursue the limited data available to them," the source says. "It's something we've been calling for them to do."

The agency's assessments of ETBE and DCE do not include cancer safety standards because the agency determined it did not have the necessary data to calculate these numbers. But the agency performed a weight of evidence analysis for declaring whether the chemicals are carcinogenic -- a determination that can result in consumer deselection -- including Ramazzini data. EPA's draft assessments of acrylonitrile and MTBE have yet to be publicly released, so it is unknown to what extent those rely, or relied, on Ramazzini data.

The Ramazzini data has proven controversial largely because its methods differ greatly from U.S. counterparts. EPA and other federal agencies tend to use lab rodent studies of specific duration -- generally two years -- to make decisions about chronic exposure to chemicals. They also often use pathogen-free strains of animals in labs with pathogen barriers, to avoid confounding infections. The

Ramazzini labs have a totally different perspective. Soffritti told *Inside EPA* last spring that his lab's study design -- eschewing pathogen-free animals and facilities and allowing the animals to die naturally -- better mimics human life. American critics, however, argue that these decisions lead to confounding. In recent years, industry consultant George Cruzan and EPA scientists have authored several papers with competing explanations for an infection or lack of infection in the Ramazzini rats' lungs. Some industry sources have even suggested that the location of the Ramazzini lab, housed in a fifteenth century castle, could exacerbate the lab animals' respiratory infections. -- *Maria Hegstad*

Elizabeth Erwin  
Communications Assistant  
National Center for Environmental Assessment  
Office of Research and Development  
U.S. Environmental Protection Agency  
Office: (703) 347-0205  
Fax: (703) 347-8699